Amendments to the Specification

Please amend the paragraph on page 5, lines 21-28, as follows:

FIG. 1 (A) schematizes the protein domain structure of human POSHL1, FIG. 1 (B) shows the alignment of the RING domain of POSHL1 (SEQ ID NO: 4164) with that of other proteins (SEQ ID NO: 4165 for 1G25_A, SEQ ID NO: 4166 for gi 2145348, SEQ ID NO: 4167 for gi 2342720, SEQ ID NO: 4168 for gi 2738440, SEQ ID NO: 4169 for gi 3043558, SEQ ID NO: 4170 for gi 3152606, SEQ ID NO: 4171 for gi 3002588, and SEQ ID NO: 4172 for gi 6226931), as well as the consensus sequence (SEQ ID NO: 4163), FIG. 1 (C) shows the alignment of the first SH3 domain of POSHL1 (SEQ ID NO: 4174) with that of other proteins (SEQ ID NO: 4175 for 1PHT, SEQ ID NO: 4176 for gi 3882275, SEQ ID NO: 4177 for gi 4176446, SEQ ID NO: 4178 for gi 2114412, SEQ ID NO: 4179 for gi 2190355, SEQ ID NO: 4180 for gi 4894215, SEQ ID NO: 4181 for gi 3158515, and SEQ ID NO: 4182 for gi 3002588), as well as the consensus sequence (SEQ ID NO: 4173), FIG. 1 (D) shows the alignment of the second SH3 domain of POSHL1 (SEQ ID NO: 4184) with that of other proteins (SEQ ID NO: 4185 for 1PHT, SEQ ID NO: 4186 for gi 3880771, SEQ ID NO: 4187 for gi 729368, SEQ ID NO: 4188 for gi 1346669, SEQ ID NO: 4189 for gi 2961227, SEQ ID NO: 4190 for gi 2960022, SEQ ID NO: 4191 for gi 3002588, and SEQ ID NO: 4192 for gi 3599478), as well as the consensus sequence (SEQ ID NO: 4183), and FIG. 1 (E) shows the alignment of the third SH3 domain of POSHL1 (SEQ ID NO: 4194) with that of other proteins (SEQ ID NO:

4195 for 1PHT, SEQ ID NO: 4196 for gi 4322306, SEQ ID NO: 4197 for gi 127962, SEQ ID NO: 4198 for gi 7619882, SEQ ID NO: 4199 for gi 3170194, SEQ ID NO: 4200 for gi 3002588, SEQ ID NO: 4201 for gi 13324869, and SEQ ID NO: 4202 for gi 488296), as well as the consensus sequence (SEQ ID NO: 4193);

Please replace the paragraph on page 6, line 20, through page 7, line 2, with the following amended paragraph:

Like mouse POSH protein, human POSHL1 has one N-terminal RING finger domain and several SH3 domains (three SH3 domains for POSHL1 and four for POSH). In POSHL1, the RING finger domain occurs at residues 12 – 52 and the three SH3 domains occur at residues 126 - 182, 188 - 249, and 381 - 439 respectively (~~http://www.ncbi.nlm.nih.gov/Structure/cdd~~National Center for Biotechnology Information (NCBI) conserved domain search website, Altschul *et al.*, Nucleic Acids Res., 25:3389-3402 (1997)). E3 ubiquitin-protein ligase activity is intrinsic to the RING finger domain of c-Cbl and is likely to be a general function of this domain. Various RING finger domains exhibit binding activity towards E2 ubiquitin-conjugating enzymes (Ubc' s). SH3 (Src homology 3) domains are often indicative of a protein involved in signal transduction related to cytoskeletal organization. SH3 domain was first described in the Src cytoplasmic tyrosine kinase. The structure of SH3 is a partly opened beta barrel.

Please replace the paragraph on page 7, lines 3-12, with the following amended paragraph:

Other signatures of the newly isolated POSHL1 proteins were identified by searching the PROSITE database (Expert Protein Analysis System (ExPASy) web site~~http://www.expasy.ch/tools/scnpsit1.html~~). These include four N-glycosylation sites (250-253, 270-273, 281-284, and 519-522), two cAMP- and cGMP-dependent protein kinase phosphorylation sites (441-444 and 704-707), fifteen Protein kinase C phosphorylation sites, nine Casein kinase II phosphorylation sites, a single tyrosine kinase phosphorylation site (155-163), twelve N-myristoylation site, and a single amidation site (98-101).

Please replace the paragraph on page 19, lines 16-28, with the following amended paragraph:

For purposes herein, percent identity of two nucleic acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at the National Center for Biotechnology Information (NCBI) web site.

~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html.~~

To assess percent identity of nucleic acids, the BLASTN module of BLAST 2 SEQUENCES is used with default values of (i) reward for a match: 1; (ii) penalty for a

mismatch: -2; (iii) open gap 5 and extension gap 2 penalties; (iv) gap X_dropoff 50 expect 10 word size 11 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 73, lines 4-10, with the following amended paragraph:

Bacterial cells can be rendered electrocompetent — that is, competent to take up exogenous DNA by electroporation — by various pre-pulse treatments; vectors are introduced by electroporation followed by subsequent outgrowth in selected media. An extensive series of protocols is provided online in Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735, BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~.

Please replace the paragraph on page 74, lines 13-31, with the following amended paragraph:

For chemical transfection, DNA can be coprecipitated with $CaPO_4$ or introduced using liposomal and nonliposomal lipid-based agents. Commercial kits are available for $CaPO_4$ transfection (CalPhos™ Mammalian Transfection Kit, Clontech Laboratories, Palo Alto, CA, USA), and lipid-mediated transfection can be practiced using commercial reagents, such as LIPOFECTAMINE™ 2000, LIPOFECTAMINE™ Reagent, CELLFECTIN® Reagent, and LIPOFECTIN® Reagent (Invitrogen, Carlsbad, CA, USA), DOTAP Liposomal Transfection Reagent, FuGENE 6, X-tremeGENE Q2, DOSPER,

(Roche Molecular Biochemicals, Indianapolis, IN USA), Effectene™, PolyFect®, Superfect® (Qiagen, Inc., Valencia, CA, USA). Protocols for electroporating mammalian cells can be found online in Electroprotocols Online: Collection of Protocols for Gene Transfer (Bulletin #1029735, BioRad, Richmond, CA, USA) ~~(http://www.bio-rad.com/LifeScience/pdf/New_Gene_Pulser.pdf)~~. *See also*, Norton *et al.* (eds.), Gene Transfer Methods: Introducing DNA into Living Cells and Organisms, BioTechniques Books, Eaton Publishing Co. (2000) (ISBN 1-881299-34-1), incorporated herein by reference in its entirety.

Please replace the paragraph on page 76, lines 13-25, with the following amended paragraph:

For purposes herein, percent identity of two amino acid sequences is determined using the procedure of Tatiana *et al.*, "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", *FEMS Microbiol Lett.* 174:247-250 (1999), which procedure is effectuated by the computer program BLAST 2 SEQUENCES, available online at the National Center for Biotechnology Information (NCBI) web site.

~~http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html,~~

To assess percent identity of amino acid sequences, the BLASTP module of BLAST 2 SEQUENCES is used with default values of (i) BLOSUM62 matrix, Henikoff *et al.*, *Proc. Natl. Acad. Sci. USA* 89(22):10915-9 (1992); (ii) open gap 11 and extension gap 1

penalties; and (iii) gap x_dropoff 50 expect 10 word size 3 filter, and both sequences are entered in their entireties.

Please replace the paragraph on page 128, lines 29-33, with the following amended paragraph:

Motif searches using Pfam (Washington University, St. Louis, web site) ~~(http://pfam.wustl.edu)~~, SMART (European Molecular Biology Laboratory, Heidelberg, web site) ~~(http://smart.embl-heidelberg.de)~~, and PROSITE pattern and profile databases (Expert Protein Analysis System (ExPASy) web site) ~~(http://www.expasy.ch/prosite)~~, identified several known domains shared with mouse POSH protein.

Please replace the paragraph on page 129, lines 10-24, with the following amended paragraph:

Like mouse POSH protein, human POSHL1 has one N-terminal RING finger domain and several SH3 domains (three SH3 domains for POSHL1 and four for POSH). In POSHL1, the RING finger domain occurs at residues 12 – 52 and the three SH3 domains occur at residues 126 - 182, 188 - 249, and 381 - 439 respectively ~~(http://www.ncbi.nlm.nih.gov/Structure/cdd)~~ (National Center for Biotechnology Information (NCBI) conserved domain search website, Altschul *et al.*, Nucleic Acids Res., 25:3389-3402 (1997)). E3 ubiquitin-protein ligase activity is intrinsic to the RING finger domain of c-Cbl and is likely to be a general function of this domain. Various

RING finger domains exhibit binding activity towards E2 ubiquitin-conjugating enzymes (Ubc' s). SH3 (Src homology 3) domains are often indicative of a protein involved in signal transduction related to cytoskeletal organization. SH3 domain was first described in the Src cytoplasmic tyrosine kinase. The structure of SH3 is a partly opened beta barrel.

Please replace the paragraph on page 129, line 25, through page 130, line 2, with the following amended paragraph:

Other signatures of the newly isolated POSHL1 proteins were identified by searching the PROSITE database (Expert Protein Analysis System (ExPASy) web site) ~~(http://www.expasy.ch/tools/scnpsit1.html)~~. These include four N-glycosylation sites (250-253, 270-273, 281-284, and 519-522), two cAMP- and cGMP-dependent protein kinase phosphorylation sites (441-444 and 704-707), fifteen Protein kinase C phosphorylation sites, nine Casein kinase II phosphorylation sites, a single Tyrosine kinase phosphorylation site (155-163), twelve N-myristoylation site, and a single amidation site (98-101).

Please replace the paragraph on page 130, lines 13-20, with the following amended paragraph:

Transcription factor binding sites were identified using a web based program (GenomeNet website, Kyoto University Bioinformatics Center) ~~(http://motif.genome.ad.~~

~~jp/~~), including binding sites for HSF (132-136, 388-392, 624-628, 770-774, and 856-860), GATA-2 (290-299 and 576-585), GATA-3 (290-299 and 576-585), Lmo2 (291-299 and 576-584), NIT2 (93-98, 369-374, 371-376, and 579-584), Lyf1 (32-40), CdxA (322-328, 387-393, and 735-741, with numbering according to SEQ ID NO: 28), amongst others.

Please add the following new text on page 132, beginning on line 1, as follows:

SEQ ID NO: 4163 (aa, consensus sequence of the Ring Domain)

SEQ ID NO: 4164 (aa, aa 12-52 portion of POSHL1)

SEQ ID NO: 4165 (aa, aa 6-49 portion of 1G25_A)

SEQ ID NO: 4166 (aa, aa 18-56 portion of gi 2145348)

SEQ ID NO: 4167 (aa, aa 91-132 portion of gi 2342720)

SEQ ID NO: 4168 (aa, aa 111-145 portion of gi 2738440)

SEQ ID NO: 4169 (aa, aa 71-111 portion of gi 3043558)

SEQ ID NO: 4170 (aa, aa 91-132 portion of gi 3152606)

SEQ ID NO: 4171 (aa, aa 111-145 portion of gi 3002588)

SEQ ID NO: 4172 (aa, aa 71-111 portion of gi 6226931)

SEQ ID NO: 4173 (aa, consensus sequence of the SH3 Domain 1)

SEQ ID NO: 4174 (aa, aa 126-183 portion of POSHL1)

SEQ ID NO: 4175 (aa, aa 4-78 portion of 1PHT)

SEQ ID NO: 4176 (aa, aa 864-921 portion of gi 3882275)

SEQ ID NO: 4177 (aa, aa 509-566 portion of gi 4176446)

SEQ ID NO: 4178 (aa, aa 994-1049 portion of gi 2114412)

SEQ ID NO: 4179 (aa, aa 244-302 portion of gi 2190355)

SEQ ID NO: 4180 (aa, aa 113-172 portion of gi 4894215)

SEQ ID NO: 4181 (aa, aa 383-440 portion of gi 3158515)

SEQ ID NO: 4182 (aa, aa 135-192 portion of gi 3002588)

SEQ ID NO: 4183 (aa, consensus sequence of the SH3 Domain 2)

SEQ ID NO: 4184 (aa, aa 188-251 portion of POSHL1)

SEQ ID NO: 4185 (aa, aa 4-78 portion of 1PHT)

SEQ ID NO: 4186 (aa, aa 408-466 portion of gi 3880771)

SEQ ID NO: 4187 (aa, aa 153-210 portion of gi 729368)

SEQ ID NO: 4188 (aa, aa 458-515 portion of gi 1346669)

SEQ ID NO: 4189 (aa, aa 995-1052 portion of gi 2961227)

SEQ ID NO: 4190 (aa, aa 3-60 portion of gi 2960022)

SEQ ID NO: 4191 (aa, aa 197-258 portion of gi 3002588)

SEQ ID NO: 4192 (aa, aa 1160-1215 portion of gi 3599478)

SEQ ID NO: 4193 (aa, consensus sequence of the SH3 Domain 3)

SEQ ID NO: 4194 (aa, aa 381-440 portion of POSHL1)

SEQ ID NO: 4195 (aa, aa 4-78 portion of 1PHT)

SEQ ID NO: 4196 (aa, aa 664-723 portion of gi 4322306)

SEQ ID NO: 4197 (aa, aa 107-164 portion of gi 127962)

SEQ ID NO: 4198 (aa, aa 126-183 portion of gi 7619882)

SEQ ID NO: 4199 (aa, aa 156-213 portion of gi 3170194)

SEQ ID NO: 4200 (aa, aa 453-512 portion of gi 3002588)

SEQ ID NO: 4201 (aa, aa 380-436 portion of gi 13324869)

SEQ ID NO: 4202 (aa, aa 42-104 portion of gi 488296)

At the end of the written description, before the claims, please delete the previously submitted "Sequence Listing" and insert the revised "Sequence Listing" which is contained in electronic format only on the accompanying compact discs.